

# HISTOPATHOLOGICAL EVALUATION OF GALL BLADDER IN CHOLECYSTECTOMY SPECIMENS IN A TERTIARY HEALTH CARE CENTRE OF NEPAL

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## ABSTRACT

Gall bladder is one of the important digestive organ which encountered with different histopathological changes. Different changes in dietary habit, obesity, oral contraceptives, alcohol have shows increased pattern of cholecystitis and cholelithiasis and other pathological findings. Detail examination of gall bladder in cholecystectomy specimen helps to evaluate different histopathological pattern of gall bladder lesion and also help to differentiate non-neoplastic from neoplastic lesion and also helps in further management. This was a cross sectional study done in the Department of Pathology, Nepal Medical College Teaching Hospital, Kathmandu, Nepal, during the study of period of six months (February 2020 to July 2020). A total of 127 patients between 16 years to 63 years with mean age of  $40.54 \pm 10.88$  years. There were 127 cholecystectomy specimens were received during study period and out of which 94 were female and 33 were male. On histopathological evaluation, chronic cholecystitis was most common findings followed by chronic cholecystitis with cholesterolosis. Other findings were chronic cholecystitis with adenomyosis, chronic cholecystitis with pyloric metplesia, chronic cholecystitis with intestinal metpalsia, chronic cholecystitis with polyp, acute on chronic cholecystitis, Xanthogranulomatous cholecytsitis and adenocarcinoma . Median age was 40.54 years. It was concluded that Chronic cholecystitis was the most common histopathological findings and the common groups was 41-50 years. Routine examination of cholecystectomy specimens grossly and microscopically is important for patient management Though a very few cases of carcinoma of Gall bladder is seen, it is very important to make sure that all cholecystectomy specimens undergone histopathological examination, with this, we can achieve timely diagnosis and early managements.

## KEYWORDS

Gall bladder, cholecystectomy, cholecystitis, cholesterolosis, metaplasia, Nepal

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## INTRODUCTION

Gallbladder is the organ of digestive system which is mostly encountered with different histopathological changes including acute or chronic inflammation, mucosal changes, infection, benign polyps, premalignant and malignant conditions.<sup>1</sup> In the recent decades, changes in dietary pattern with high calorie and high fat diet, sedentary lifestyles, obesity, oral contraceptives, alcohol consumption has shown the increased pattern of cholecystitis and cholelithiasis.<sup>2,3</sup> Besides cholelithiasis and cholecystitis, the distribution of benign gallbladder diseases is quite diverse including acalculous conditions such as acalculous cholecystitis, cholesterolosis, polyposis of gallbladder and calculous cholecystitis which may or may not be associated with gallstones.<sup>4</sup>

Cholecystectomy is the most commonly performed surgical procedure for gall bladder diseases and the majority of the cholecystectomies are done for cholelithiasis affecting 10% to 20% of adult population in developed countries.<sup>5</sup> More than 95% of biliary tract disease is attributed to cholelithiasis and its prevalence increases with age from 21 to 80 years and higher in females than males whereas gallbladder cancer is the most common malignancy of the extra hepatic biliary tract.<sup>6,7</sup>

Surgical removal of gall bladder is common and the cholecystectomized gall bladder specimens are one of the frequently received specimens in the department of Pathology. Because of the various findings in the gall bladder diseases this study is designed to evaluate the histopathological patterns of gall bladder lesions and to determine the demographic characteristics of the patients.

## MATERIALS AND METHODS

The study was carried out on 127 cholecystectomy specimens received in the Department of Pathology, Nepal Medical College Teaching Hospital (NMCTH), Attarkhel, Gokarneshwor-8, Kathmandu, Nepal between February 2020 and July 2020. Information regarding age, gender, site of biopsy and other relevant clinical data were collected from requisition form from the Surgical Department, NMCTH. All cholecystectomy specimens received in the Pathology Department were included in the study whereas persons with previous history of radiotherapy and chemotherapy were excluded from the study. Ethical approval from Institutional Review Committee, NMCTH was taken.

The tissue samples received in 10.0% buffered formalin were grossly and histologically observed in Pathology Department as per standard guidelines. Multiple sections were taken from the specimens and submitted for processing by paraffin embedding. Appropriate sections of 4-5micron thick tissue sections were cut and stained routinely with Hematoxylin and Eosin (H and E) stain, mounted in DPX and examined under the microscope.

On microscopy, mucosa was examined for inflammation, cholesterolosis, intestinal and pyloric metaplasia, adenomyosis, polyp and carcinoma. The presence of inflammation (acute/chronic/eosinophilic/xanthogranulomatous), muscle hypertrophy, fibrosis and glandular infiltrations in gall bladder wall were noted.

The following microscopic diagnostic features were used for the final histopathological diagnosis:

- *Cholesterolosis*: Cholesterol aggregation with yellowish streaks, foamy macrophages in lamina propria
- *Pyloric metaplasia*: Few pyloric glands in lamina propria
- *Intestinal metaplasia*: Presence of goblet cells
- *Adenomyosis*: Few glands in lamina propria
- *Polyp*: Polypoidal lesions in the inner gall bladder wall
- *Xanthogranulomatous*: lipid laden macrophages forming nodules or streaks in gall bladder wall
- *Carcinoma*: Infiltration of malignant glandular epithelium into muscle layer

The microscopic findings were noted and histopathological diagnosis was done. The data obtained were managed in MS Excel 2016 and later analyzed using IBM SPSS version 20. The histopathological spectrum of gall bladder lesions were determined based on the demographic characteristics of the patients.

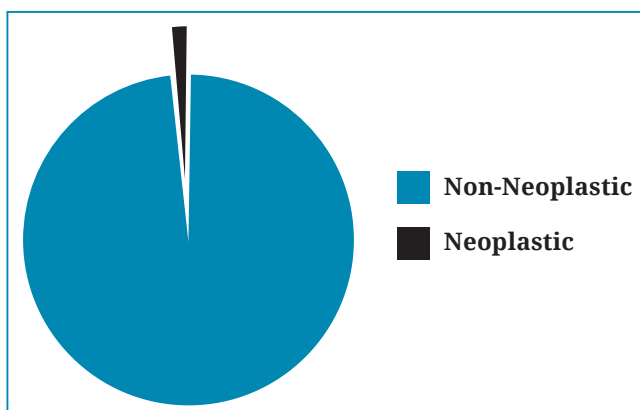
## RESULTS

A total of 127 cholecystectomy specimens were received during the study period. Of those 127 patients, 94 (74.0%) were female and 33 (26.0%) were male with M: F ratio 1:2.8. The age group was ranging from 16 years to 63 years with mean age of 40.54 years (SD=10.88) and the maximum gall bladder lesions were observed in males and females of age group 41 to 50 years (Table 1).

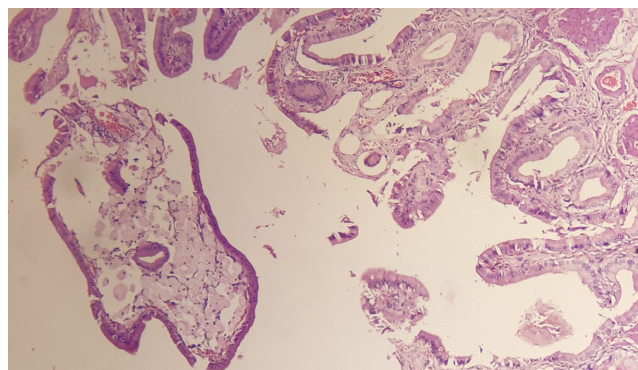
**Table 1: Age and gender wise distribution**

Age Group (years)	M (n)	F (n)	Total (n/%)
11-20	2	3	5 (3.9%)
21-30	5	15	20(15.7%)
31-40	6	25	31(24.4%)
41-50	14	29	43(33.9%)
51-60	5	18	23(18.1%)
61-70	1	4	5(3.9%)
<b>Total</b>	<b>33 (26%)</b>	<b>94 (74%)</b>	<b>127 (100.0%)</b>

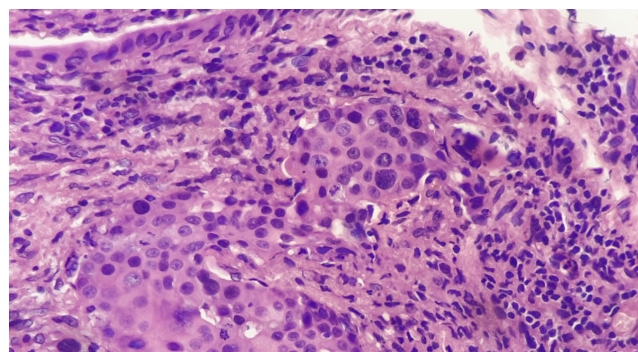
Out of 127 cholecystectomy specimens, on histopathological examination, 125 (98.4%) specimens showed non-neoplastic pathology whereas 2 (1.6%) specimens were present with neoplastic features (Fig. 1).



**Fig. 1:** Neoplastic and non-neoplastic distribution of specimens



**Fig. 2:** Gallbladder Cholesterosis (10x)



**Fig. 3:** Adeno carcinoma of gallbladder (40x)

Among non-neoplastic specimens, chronic cholecystitis was found to be the most predominant type accounting 87 cases (68.50%) of inflammatory lesions followed by cholesterosis (Fig. 2) which was observed in 10(7.87%) cholecystectomy specimens. Chronic cholecystitis with adenomyosis and pyloric metaplasia each were diagnosed in 8 (6.3%) cases. Similarly, chronic cholecystitis

**Table 2: Distribution of histopathological pattern in cholecystectomy specimens**

Histopathological Diagnosis		n	%
Non-Neoplastic (n=125)	Chronic Cholecystitis	87	68.50
	Chronic Cholecystitis with Cholesterosis	10	7.87
	Chronic Cholecystitis with Adenomyosis	8	6.30
	Chronic Cholecystitis with Pyloric Metaplasia	8	6.30
	Chronic Cholecystitis with Intestinal Metaplasia	4	3.15
	Chronic Cholecystitis with Polyp	4	3.15
	Acute on Chronic Cholecystitis	3	2.36
	Xanthogranulomatous cholecystitis	1	0.79
Neoplastic (n=2)	Adenocarcinoma of Gall bladder	2	1.58
<b>Total</b>		<b>127</b>	<b>100</b>



with intestinal metaplasia and polyps were seen in 4 (3.1%) cases. Acute/active on chronic cholecystitis was observed in 3 (2.4%) cases each. There was a single case (0.8%) of Xanthogranulomatous cholecystitis. Among the two neoplastic lesions, both the cases adenocarcinoma of gall bladder (Table 2),(Fig 3).

## DISCUSSION

Gall bladder disease is a common health issue worldwide which require surgical removal procedure, cholecystectomy. The excised gall bladder is evaluated routinely by histopathological examination and pathological features are identified. In this study we determined the histomorphological spectrum of cholecystectomy specimens and demographic characteristics of the patients.

Among 127 cholecystectomy specimens received, gall bladder lesions were predominantly observed in females as compared to males accounting 94 (74.0%) female cases and 33 (26.0%) male cases with male to female ratio (M: F) ratio of 1:2.8. Our findings were similar to the other studies who have reported male to female ratio of 1:2.12 and 1:2.06 respectively.<sup>1,3</sup>

In this study the age of patients ranged from 16 years to 63 years with mean age of 40.54±10.88 years and the majority of gall bladder lesions were observed in age group 41 to 50 years. This finding was similar to the study done by Anushree *et al*<sup>3</sup> and Kumar *et al*<sup>8</sup> who reported that most of the gall bladder lesions were seen in 4<sup>th</sup> decade to 5<sup>th</sup> decade of life. However some other studies found that 31 to 40 years as the major age group for cholecystectomy.<sup>4,9,10</sup> Contrastingly Uysal *et al*<sup>11</sup> reported maximum cholecystectomy (49%) cases in the age group more than 50 years.

In the present study, all the cholecystectomy specimens had cholecystitis with infiltrated inflammatory cells, varying clinical and pathological characteristics. Among 127 specimens examined, chronic cholecystitis was found to be the most common diagnosis (68.50% cases). Several other studies also reported chronic cholecystitis as the most common lesion in gall bladder specimens.<sup>3-6</sup> Surprisingly Uysal *et al*<sup>11</sup> and Siddiqui *et al*<sup>12</sup> observed 95% and 92% of cholecystectomy specimens diagnosed with chronic cholecystitis respectively.

Apart from chronic cholecystitis, various other histomorphological spectrum including cholesterolosis, adenomyosis, pyloric metaplasia, intestinal metaplasia,

polyps, acute on chronic cholecystitis and xanthogranulomatous cholecystitis were seen in 31-50% of cases among non neoplastic lesions. In our study, chronic cholecystitis with cholesterolosis was the second common finding accounting 10 (7.87%) of total cholecystectomy cases. Histopathological examination of cholesterolosis showed the thickened wall, aggregated cholesterol with yellowish streaks and foamy macrophages in lamina propria of gall bladder. Similar to our study Kafle *et al*<sup>10</sup> and Bhatt *et al*<sup>13</sup> also observed cholesterolosis as the second common findings of cholecystectomy specimens comprising 22% and 9.75% of total cases respectively.

In this study, 8 (6.3%) cholecystectomy cases were diagnosed chronic cholecystitis with adenomyosis which were presented with thickened wall and glands infiltrated into the lamina propria of gall bladder. A study by Ganguly *et al*<sup>7</sup> reported 5% cases of gall bladder specimens with adenomyotic features comprising 3% adenomyomatosis gall bladder and 2% adenomyomatous polyp respectively.

A total of 8 (6.3%) gall bladder cases were diagnosed chronic cholecystitis with pyloric metaplasia showing characteristic feature of thickened wall and pyloric glands infiltrated into lamina propria causing perineural and intraneural invasion. In contrast to our study, Kafle *et al*<sup>10</sup> found 33% of gastric metaplasia in cholecystectomy specimens.

Out of 127 specimens, 4 (3.15%) cholecystectomies were found to be chronic cholecystitis with intestinal metaplasia featuring thickened wall and presence of goblet cells. In both the studies by Kumbhakar *et al*<sup>4</sup> and Medhi *et al*<sup>14</sup>, intestinal metaplasia was diagnosed in 0.25% of gall bladder cases whereas Kafle *et al*<sup>10</sup> found 8% of gall bladder specimens with intestinal metaplasia which was two times more cases than we observed.

In the present study, 4 (3.15%) cholecystectomy specimens were diagnosed chronic cholecystitis with polyps, presented with polypoidal lesions in the inner gall bladder wall. Other studies by Selvi *et al*<sup>6</sup>, Ganguly *et al*<sup>7</sup> and Bhatt *et al*<sup>13</sup> reported fewer incidence of cholecystitis with polyps accounting 2.5%, 2% and 1.74% of total cholecystectomy specimens respectively.

In our study, 3 (2.36%) cases had acute on chronic cholecystitis with specific microscopic features of hemorrhage, presence of extensive neutrophils and fibrinoid materials. Contrastingly, Beena *et al*<sup>9</sup> and Kafle *et al*<sup>10</sup> reported nearly three times more incidence, 10.5% and 8% of total cases, as acute on chronic cholecystitis.

A single case (0.79%) of Xanthogranulomatous cholecystitis was seen in a 36 years old female. Histopathological examination showed marked wall thickening and the lipid laden macrophages forming streaks or nodules in gall bladder wall. Similar to our study, Selvi et al<sup>6</sup> and Uysal et al<sup>11</sup> found a single case of Xanthogranulomatous cholecystitis among cholecystectomy specimens whereas Ganguly et al,<sup>7</sup> Kafle et al,<sup>10</sup> and Kumar et al<sup>15</sup> observed more cases than us accounting 4%, 6% and 1.92% of total cholecystectomy specimens.

The remaining 2 (1.58%) specimens were found to be neoplastic diagnosed as adenocarcinoma featured with a mass, thickened wall, hemorrhagic and glandular infiltration into the muscular layer. One case occurred in female patient of 56 years whereas other in male patient of 49 years. Our finding was similar to

Kumbhakar et al<sup>4</sup> and Kumar et al<sup>15</sup> accounting 1.25% and 1.92% respectively whereas Siddiqui et al<sup>12</sup> and Tiwari et al<sup>16</sup> observed 6 and 10 cases as incidental carcinoma of gall bladder.

The study concludes that females of age group 41-50 years usually undergo cholecystectomy. Chronic cholecystitis was the most common histopathological diagnosis followed by cholesterolosis, adenomyosis, metaplasia, acute on chronic cholecystitis, polyps, adenocarcinoma and xanthogranulomatous cholecystitis. Routine histopathological examination of cholecystectomy specimens is important to detect non neoplastic lesions as well as neoplastic lesions and sometimes incidental gall bladder cancer. Hence, we recommend comprehensive histopathological examination of all gall bladder samples for timely diagnosis and quick intervention.

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